# Characterisation of mechanical properties of human pulmonary and aortic tissue

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*Abstract*— **The aim of this study is to characterise the mechanical properties of aortic and pulmonary arterial tissue, thereby comparing both tissue types and investigating the effect of lung-affecting disease on the mechanical behaviour of pulmonary arteries. Force-controlled, planar biaxial tensile tests were performed on human tissue samples collected from donors and receptors undergoing lung transplantation. In total 8 pulmonary donor, 6 pulmonary receptor and 6 aortic donor samples were tested and analysed. Donor samples are considered to be healthy, while receptors provided pathological tissue. The stiffness and strength of each sample were calculated from the stress-strain curves and a statistical analysis was performed between the three tissue groups (pulmonary donor, pulmonary receptor and aortic donor). The stiffness of aortic donor tissue was found to be significantly higher than for pulmonary donor tissue ($p < 0.01$) at physiological systolic stresses. The same could be observed for the strength ($p < 0.05$). Pulmonary samples were, however, significantly stiffer than aortic samples at stresses in the physiological range of aorta ($p < 0.01$). There was no significant difference found between the donors and receptors for pulmonary samples. The fact that the physiological pressure in the aorta is fivefold higher than in the pulmonary artery is also reflected in its stiffness and strength.**

*Keywords*— **pulmonary artery, aorta, biaxial testing, mechanical properties**

## I. Introduction

Until present, knowledge about the mechanical properties of human cardiovascular tissue is limited. Most studies focus on aorta, in which case the aim is not to investigate the mechanical behaviour of the tissue of interest as such, but to evaluate the effect of pathologies such as aneurysm formation [1] or the effect of ageing [2]. On human pulmonary arteries, literature does not offer much information. [3] investigates the dilatation of the aortic root after the Ross procedure, but the focus here is more on the root and the valves of both the pulmonary artery and the aorta and hence again not on the mechanical properties of the vessel wall. On the other hand, animal pulmonary tissue has been studied more, e.g. [4] studied canine pulmonary arteries. [5] compared the mechanical properties of 4 ovine pulmonary arterial samples with 1 paediatric sample. This paper also clearly points out how the interspecies variation in mechanical properties is often disregarded in e.g. stent design, causing them to function suboptimally or even damage the vessel wall.

The design of surgical robotic equipment is a field of study that can benefit from knowledge of the mechanical properties of soft biological tissue. The robotic devices currently used in the operating theatre do not provide haptic feedback, e.g. the Da Vinci robot (Intuitive surgical®). The risk for tissue damage is not negligible, which is why the implementation of a tissue overload prevention mechanism, based on biomechanical models of the manipulated tissue, is crucial [6].

Chronic Obstructive Pulmonary Disease (COPD), Cystic Fibrosis (CF) and Nonspecific Interstitial Pneumonia (NSIP) are diseases that affect lung function. One could speculate that, as a result, the heart will increase its pumping activity in order to meet the oxygen demand. The physiological pressure will rise, thus affecting the structure of the arterial wall and hence the mechanical properties. However, to the authors's knowledge, literature provides no data on this matter.

The examples above show a growing demand for data on the mechanical properties of human cardiovascular tissue. Animal tissue data is omnipresent, but similar human data is not. The goal of this research is to provide insight into the mechanical properties of human cardiovascular tissue. Stiffness and strength of the tissue samples will be analysed. Two hypotheses are investigated. Firstly, aortic tissue is stiffer than pulmonary arterial tissue at physiological loading conditions. Secondly, due to the effect of the lung-affecting diseases, the pulmonary receptors are stiffer than pulmonary donors.

In the following sections, the experimental protocol and the calculations of the mechanical properties are explained. Next, the obtained results are reported and discussed.

## II. Materials and Methods

### A. Sample collection and preparation

14 pulmonary samples were tested, 8 from donors (age 40.9 ± 18.3 years, BMI 23.0 ± 2.8, 5 male/3 female) and 6 from receptors (age 47.7 ± 11.3 years, BMI 21.5 ± 5.7,

2 male/4 female). 6 aortic donor samples (age 38.8 $\pm$ 14.3 years, BMI 26.4 $\pm$ 5.14, 5 male/1 female) were tested. Donor tissue is assumed to be healthy. This is merely an assumption since no background information of the donor samples was provided, only that they were suitable for implantation. Receptors suffered from diseases affecting lung function, such as COPD (4 samples), CF (1 sample) and NSIP (1 sample). This study was approved by the ethical committee of University Hospital Leuven (s51577).

The pulmonary samples were harvested form a location close to the pulmonary valves. Immediately after excision, the samples were dry-frozen. Concerning the aortic samples: the full aortic arch was harvested and frozen in a 0.9 % NaCl solution immediately after excision. All samples were thawed in a refrigerator at $4°C$ and square samples with a side of 7 mm were cut. The circumferential and longitudinal direction were derived from the morphology of the samples. As markers, five fragments of surgical suture wire were attached to tissue in the most homogeneous region. The thickness of the samples was measured via image analysis of a picture of the tissue placed between two metal plates with known thicknesses.

### *B. Biaxial Testing*

Cardiovascular tissue is anisotropic, non-linear and undergoes high deformations. This is a consequence of the heterogeneity of the vessel wall (see e.g. [7] for a more detailed description). Due to the complexity of the tissue, biaxial experiments, allowing loading in different directions, are necessary to fully characterise its mechanical properties.

The experiments were performed on a BioTester (CellScale, Waterloo, Canada). This device has two axes with two actuators and one force cell per axis. The square samples were mounted with 4 BioRakes. The two pairs of actuators are operated independently, so that is possible to apply different stretch or force ratios. One BioRake consists of five hooks spaced by 1 mm. The circumferential direction of the sample and the x-axis of the device were aligned.

The pulmonary samples were tested with 2.5 N load cells and the aortic samples with 23 N load cells. Both load cells have an accuracy of 0.2 % of the full scale. During the experiment, the samples were submerged in a 0.9% NaCl solution at room temperature. A CCD camera with a resolution of 1280 pixels by 960 pixels, monitored the deformation process. The sampling rate was 30 Hz for the force measurements and 15 Hz for the CCD camera. The loading rate was 0.14 N/s for the pulmonary samples and 0.47 N/s for the aortic samples.

The experiments on both the pulmonary and aortic samples were conducted under a force controlled protocol. 10 preconditioning cycles at preliminary evaluated physiological forces were used. The physiological forces were derived from the circumferential wall stress at systolic pressure. According to [8] the systolic pressure in the pulmonary artery is 25 mmHg and 120 mmHg in the aorta. With Laplace's law, the circumferential stress was estimated to be 31 kPa in the pulmonary artery and 70 kPa in the aorta, the corresponding estimated wall thicknesses were 1.33 mm and 4 mm respectively. These values correspond well with the values reported in [3], 22 kPa for the pulmonary artery and 73 kPa for the aorta. From these stresses, a physiological force of 0.208 N for pulmonary arteries and of 1.4 N for aorta were derived. After preconditioning, the sample underwent several test sequences. Each test sequence was performed at a different force-level. For every force-level, three sets of five cycles were conducted, each set with a different ratio of the force in the x- and y-direction: $F_x : F_y$ = 1:0.5, 1:1, 0.5:1.

From preliminary experiments, it was determined that pulmonary samples can endure forces of up to 10 times the physiological force, i.e. 2.08 N. Therefore, the protocol for pulmonary samples consists of 6 test sequences. The force in the first test sequence is equal to the physiological force, followed by test sequences at 2, 4, 6, 8 and 10 times the physiological force. The aortic samples are able to withstand forces of up to 4 times the physiological force, i.e. 5.6 N. The protocol for the aortic samples counts 3 test sequences: physiological force, 2 times and 4 times the physiological force.

### *C. Calculation of stiffness and strength*

From the force-measurements, the first Piola-Kirchhoff stress ($P$) was calculated as the force divided by the initial cross section. On each image from the CCD-camera, the coordinates of the markers were tracked. From this data, the displacements and stretches ($\lambda_i = l_i/l_{0,i}$, with $l_i$ the current length in the i'th direction and $l_{0,i}$ the original length in the i'th direction) were calculated. As such, the gradient deformation tensor ($F$) can be constructed. This is a diagonal tensor with the diagonal elements equal to the stretches. Incompressibility and absence of shear forces were assumed. With the information of $F$ and $P$, the Cauchy stress ($\sigma$) and the second Piola-Kirchhoff stress ($S$) were calculated:

$$\sigma = J^{-1}\mathbf{F}.\mathbf{P}, \qquad \mathbf{S} = \mathbf{P}.\mathbf{F}^{-T}. \tag{1}$$

J represents the Jacobian determinant of $\mathbf{F}$. Two strain measurements were used, the engineering strain ($e$) and the Green strain ($E$) (with $\mathbf{I}$ the unity tensor):

$$\mathbf{e} = \mathbf{F} - \mathbf{I}, \qquad \mathbf{E} = \frac{1}{2}(\mathbf{F}^T.\mathbf{F} - \mathbf{I}). \tag{2}$$

The stiffness calculations were based on the Cauchy stress vs. engineering strain data from the equibiaxial protocol for a supra-physiological load level. Around a predefined stress, four points were chosen. The slope of the line interpolating these points is defined as a tissue stiffness measure.

The stiffness was evaluated at two different stress levels: the circumferential stress corresponding to diastolic and systolic pressure. For the pulmonary samples these two stress values were estimated to be 10 kPa and 31 kPa respectively. For aortic samples they were estimated to be 62 kPa and 93 kPa respectively. An extra stiffness-evaluation was done for the pulmonary donor samples, namely at a stress corresponding to the aortic systolic pressure, 120 mmHg. At that pressure, the circumferential stress in the pulmonary artery is 150 kPa according to Laplace's law for a wall thickness of 1.33 mm. This allowed to evaluate the behaviour of the pulmonary artery when put in aortic position, similar to the Ross procedure. Cauchy stress-strain curves were created for both the circumferential and longitudinal direction. Therefore the stiffness of a sample was characterised by four values: a systolic and diastolic stiffness in the x- and y-direction.

Due to biaxial loading, the strength of the sample cannot be described with one parameter. In this study the energy-concept was chosen instead. The fracture energy was calculated as the sum of the product of the maximum of the stress-strain curves (S vs. E) for both directions, as follows:

$$Energy = S_x E_x + S_y E_y \tag{3}$$

Note that, because the samples were mounted with hooks piercing through the tissue, the tissue fails at the level of these hooks and not in the middle region. Therefore, the calculated energy underestimates the real fracture energy.

### *D. Statistical analysis*

The stiffness and strength values for the pulmonary donor, receptor and aortic donor samples were compared in a one-way ANOVA (fixed effects model). A difference is statistically significant, when the p-value is lower than 0.05. The group means were compared with a t-test in case normality could be assumed. The non parametric alternative is the Kruskal-Wallis test, used when the normality assumption was not valid. For all three groups, it was also investigated whether a linear relation exists between the stiffness and other variables such as age, BMI and gender. This regression analysis was performed for systolic stiffnesses in both the x- and y- direction.

## III. Results

The average thickness of the aortic samples was 2.44 mm ($\pm$ 0.22 mm). The pulmonary donor samples were on average 1.88 mm ($\pm$ 0.38 mm) thick, the pulmonary receptor samples 1.51 mm ($\pm$ 0.5 mm). The aortic samples were significantly thicker than the pulmonary donor samples (p = 0.0074). The difference in thickness between pulmonary donors and receptors was not significant.

Table 1 summarises average stiffness values and standard deviations at physiological pulmonary and aortic stress levels and fracture energies for each group. The aortic donor samples were significantly stiffer at both diastolic and systolic stress levels, and for both directions, than the pulmonary donor samples ($p < 0.01$). When evaluating the stiffness at the aortic systolic pressure for both the pulmonary and aortic samples, the pulmonary donor samples were significantly stiffer than the aortic samples for both directions ($p < 0.01$). The difference between pulmonary donor and receptor samples was not significant. The same trend was noticed when comparing fracture energies. Aortic donor samples had a significantly higher fracture energy than pulmonary donor samples ($p < 0.05$). The difference between pulmonary donor and receptor samples on the other hand was not significant.

A linear multiple regression analysis was performed between stiffness at systolic pressure in both directions and age, BMI and gender. No dependence of stiffness on any of the variables was found for the aortic and pulmonary receptor samples. For the pulmonary donor samples, a model between stiffness and age for the x-direction (p = 0.03, $R^2$ = 0.76) and between stiffness and age and gender for the y-direction (p = 0.08, borderline significance, $R^2$ = 0.74) was found.

## IV. Discussion

The pressure in the pulmonary artery is almost fivefold higher than in the aorta. As expected, aortic tissue is significantly stiffer than pulmonary tissue at their respective physiological systolic pressure level, as depicted in Table 1. However, when considering a condition in which the pressure in both the aorta and the pulmonary artery is equal to the aortic systolic pressure, the opposite was observed: pulmonary tissue is now stiffer than aortic tissue. Indeed, in that case the pulmonary tissue is loaded under supra-physiological conditions, meaning that all collagen fibres are recruited, preventing overstretch. The aorta, on the other hand, is loaded under physiological conditions and thus not all collagen fibres are fully stretched. The findings reported in [3] confirm these results. The reported loading conditions were similar and the stiffnesses were evaluated at similar stress levels.

Table 1: The stiffness (K) at pulmonary systolic (PS), pulmonary diastolic (PD) and aortic systolic (AS) pressures in both the circumferential (x-) and longitudinal (y-) direction and the fracture energy for aortic donor (AD), pulmonary donor (PD) and receptor (PR) samples. *NE* stands for *not evaluated*.

| | | $K_{PD,x}$ [kPa] | $K_{PD,y}$ [kPa] | $K_{PS,x}$ [kPa] | $K_{PS,y}$ [kPa] | $K_{AD,x}$ [kPa] | $K_{AD,y}$ [kPa] | $K_{AS,x}$ [kPa] | $K_{AS,y}$ [kPa] | $FE$ [kJ/$m^3$] |
|---|---|---|---|---|---|---|---|---|---|---|
| AD | Average | NE | NE | NE | NE | 642.94 | 510.69 | 1002.97 | 847.40 | 664.71 |
| | Stand. Dev. | NE | NE | NE | NE | 228.35 | 124.84 | 565.77 | 312.60 | 216.98 |
| PD | Average | 148.31 | 101.55 | 241.33 | 285.27 | NE | NE | 2482.32 | 2813.42 | 423.40 |
| | Stand. Dev. | 62.33 | 61.99 | 101.44 | 168.42 | NE | NE | 946.81 | 1174.30 | 187.23 |
| PR | Average | 132.87 | 130.96 | 317.54 | 410.34 | NE | NE | NE | NE | 491.29 |
| | Stand. Dev. | 30.82 | 43.97 | 119.35 | 212.31 | NE | NE | NE | NE | 289.36 |

Surprisingly, the difference in stiffness between pulmonary donors and receptors was insignificant. Due to the pathological state, a stiffer behaviour was expected for receptor samples. However, the receptor tissue was in general not able to withstand the entire duration of the experiment, meaning that it failed at slightly lower forces than the donor samples. Though not significant, the receptor samples were in general thinner, which resulted in similar stresses. Hence, a structural difference might explain the unexpected similarity in stiffness. More tests are needed to confirm this hypothesis.

To check the effect of different displacement measurement approaches, the stiffness calculations were repeated for data based on the displacement of the BioRakes instead of on marker tracking data. The difference between the mean stiffnesses was insignificant and a strong positive correlation between the stiffness values obtained via the two methods was found. However, this does not imply that the two methods are equivalent. The method using marker tracking is recommended, since then calculations are based on data collected from the region where stresses are the most homogeneous. Calculations based on the displacements of the BioRakes, result in strain overestimations, since the displacements due to the ruptures around the rakes are taken into account as well.

The linear regression analysis did not confirm the idea that stiffness correlates with age, BMI and gender. Only for pulmonary donors a model showing that stiffness increases with age was found. The fact that a similar model was not found for aorta is most likely due to the limited amount of samples. With a larger population this trend would probably become visible. The lack of correlation between stiffness and age for pulmonary receptor samples can be explained as an effect of pathology, that most likely dominates the influence of age.

The conclusions for the fracture energy were similar to the above: no significant difference was found between pulmonary donors and receptors, but between pulmonary and aortic donors the difference was significant. Again, this can be related to the higher physiological forces that the aorta undergoes. The fact that the difference between pulmonary donors and receptors was not significant is less expected. The same remarks as for the stiffness are valid here: the receptors fail at similar stress levels as donors but the forces that they are able to endure are lower due to the lower wall thickness.

## Conflict of Interest

The authors declare that they have no conflict of interest.

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